

## Gut Check

### Do Interactions between Environmental Chemicals and Intestinal Microbiota Affect Obesity and Diabetes?

The microbiota that populate human intestinal tracts vary substantially from person to person, and mounting evidence suggests these interindividual variations in gut microbiota affect how a person metabolizes chemicals they may be exposed to. A review of the literature on this topic directed attention to a new hypothesis: that interactions between gut ecology and environmental chemicals contribute to obesity and diabetes [EHP 120(3):332–339; Snedeker and Hay]. No study has yet directly addressed that hypothesis, but this review comments on the strengths and weaknesses of studies linking environmental chemicals to obesity and diabetes and identifies gaps in the knowledge of how gut microbiota may affect the metabolism of these chemicals.

Studies reviewed by the authors found that differences in gut microbiota affected the toxicity of certain pharmaceuticals, including acetaminophen and the chemotherapy medication CPT-11. The authors propose that the same mechanisms may be at work with environmental chemicals. Enzymes produced by different gut microbe species can render ingested chemicals either more or less bioavailable, thereby affecting their toxicity. In reviewing evidence on 3 dozen



An individual's unique gut microbiota profile may affect how that person metabolizes environmental chemicals.

suspected obesogenic and diabetogenic chemicals, the authors found that at least three-quarters of them may be metabolized by gut microbe enzymes in a way that affects their absorption, distribution, metabolism, and excretion.

Human studies have shown that obese and diabetic individuals have different gut microbiota compositions than lean and nondiabetic individuals. Likewise, bariatric surgery was associated with altered gut microbiota. The composition of a gut's microbiome may influence body weight by regulating fat storage, altering the ability of the intestines to extract energy from food, and affecting satiety by modulating the levels of hormones that regulate appetite.

The reviewers also found developmental links between gut microbiota and obesity. For instance, one study connected

microbiome composition of children to their mother's weight, body mass index, and degree of weight gain during pregnancy, while another linked differences in infant microbiota composition to weight gain years later. The review highlights the importance of understanding how differences in gut microbiota might affect the fate of environmental chemicals in people and influence human health outcomes.

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## Mining Label Data

### Assessing the Presence of *ortho*-Phthalates in Pharmaceuticals and Dietary Supplements

Plasticizers known as phthalates are used in many medical and household products. They also are used in the coatings on timed-release pharmaceuticals and dietary supplements, and high levels of phthalate metabolites have been found in subjects who take such products regularly. In a new study, investigators examined available data to determine the extent and scope of *ortho*-phthalate use in pharmaceutical and dietary supplement products marketed in the United States and Canada since 1995 [EHP 120(3):379–384; Kelley et al.].

Past studies in animals have shown that some *ortho*-phthalates such as di(2-ethylhexyl) phthalate (DEHP) and di-*n*-butyl phthalate (DBP) exhibit reproductive and developmental toxicity, although no such effects were seen for diethyl phthalate (DEP). Limited data suggest that all 3 compounds may adversely affect male reproductive health in humans.

*ortho*-Phthalates are used extensively as excipients (inactive ingredients) in modified-release medications taken by mouth. These include drugs delivered through controlled release, delayed release, or targeted release systems. Depending on the product, the phthalate

coating may protect ingredients from being degraded prematurely by stomach acid, reduce stomach irritation, minimize aftertaste, or make the product easier to swallow.

In the current study, investigators searched a variety of print and electronic information sources to identify brand-name and generic medications and dietary supplements sold in the United States and Canada that contained phthalates as excipients. They identified more than 100 such products, including 50 prescription medications, 40 over-the-counter products, and 26 dietary supplements. Most of these contained DEP; 9 products contained DBP, and 1 contained both DEP and DBP.

The researchers were unable to produce a truly comprehensive list because of the lack of a centralized data retrieval source, reliance on pharmaceutical companies to accurately disclose ingredient lists for specific products, and proprietary considerations for particular formulations. However, the study does give researchers an extensive, systematically catalogued list to refer to when conducting future studies aimed at analyzing the potential risks and human health effects associated with exposure to phthalates. The authors recommend that future studies consider the amount of phthalate that is used in various forms of medicinal products in order to estimate *ortho*-phthalate exposure from these sources.

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